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| 10/033,241 | 12/28/2001 | Susan Fox Jacobsen | 00394 US1 | 8520 |

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PHARMACIA & UPJOHN
301 HENRIETTA ST
0228-32-LAW
KALAMAZOO, MI 49007

EXAMINER

COLEMAN, BRENDA LIBBY

| ART UNIT | PAPER NUMBER |
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1624

8

DATE MAILED: 07/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/033,241

Applicant(s)

JACOBSEN ET AL.

Examiner

Brenda Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2003.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☒ Claim(s) 11 and 12 is/are allowed.
6) ☒ Claim(s) 1-10 and 13-26 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-26 are pending in the application.

This action is in response to applicants' amendment filed September 15, 2003.

Claims 1, 7, 8 and 20 have been amended.

Response to Amendment

Applicant's amendments filed September 15, 2003 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 1-6, 9, 10 and 13-26 of the last office action, applicants' state that "patent applicants preferably omit what is well known in the art". However, the definition of prodrug in the specification is such that "prodrug refers to compounds that are rapidly transformed in vivo to yield the parent compound of the above formula, for example, by hydrolysis in blood".

The term prodrug is of indeterminate scope in that they vary widely from drug to drug. It is not known which moiety of formula (I) would form the basis for the prodrug. Every ester, amide and carbamate in theory is biohydrolyzable, i.e. is capable in some degree of hydrolyses. Not to mention the many in vivo environments that this occurs in. It is the Wands factors, which are used to evaluate the enablement question. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5)

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the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant invention, has claims which embrace substituted octahydroazepino[4,5-b]indole compounds. The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would not know how to prepare the various compounds suggested by claims 1-6, 9, 10 and 13-26. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

Claims 1-6, 9, 10 and 13-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled a), b), c), d), e), f) and h) maintained in the last office action, which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled g) maintained in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive.

g) The applicants' state that "determining whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification" and that "it is well known in the respective field that 5-HT ligands are effective in treating a wide range of central nervous system (CNS) disorders". However, Jones et al., Pharmacology, Biochemistry and Behavior herein provided is speculative at best with respect to the use of 5-HT6 receptor antagonists to enhance cognitive function. Jones also stated that more recently discovered 5-HT6 and 5-HT7 receptors are still being evaluated for potential therapeutic applications, so it is too early to predict how much impact they may have in the future. Thus the treatment of diseases based solely on "a medical condition for which a 5-HT6 receptor antagonist is indicated" does not provide for the treatment of every disease and/or disorder claimed herein. Additionally, the scope of diseases and/or disorders associated with serotonin receptors could alter over time. The applicants' are not entitled to preempt the efforts of others. The applicants' are only entitled to those diseases and/or disorders associated with serotonin receptors at the time of filing.

Claims 13-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

3. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 102, anticipation rejection of claims 1-7 and 13-26 labeled paragraph 3 of the last office action, which is hereby **withdrawn**.

4. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 103, obviousness rejection of claims 1-7 and 13-26 labeled paragraph 4 of the last office action, which is hereby **withdrawn**.

5. The applicant's amendments and arguments are sufficient to overcome the obviousness-type double patenting rejection of claims 1-7 and 13-26 labeled paragraph 5 of the last office action, which is hereby **withdrawn**.

In view of the amendment dated September 15, 2003, the following new grounds of rejection apply:

Specification

6. The disclosure is objected to because of the following informalities: the amendment to the specification submitted September 15, 2003 has not been entered, since there was no direction to indicate where to insert the amendment.

Appropriate correction is required.

7. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re*

Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 7 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 14-15, 22-23 and 30-31 on page 7 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- b) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 16-17, 24-25 and 32-33 on page 7 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- c) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 18-19 and 26-27 on page 7 and lines 1-2 on page 8 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- d) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 20-21 and 28-29 on page 7 and lines 3-4 on page 8 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

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e) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 6-7, 10-11 and 14-15 on page 8 of the amendment.

There is insufficient antecedent basis for this limitation in the claim.

f) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 8-9, 12-13 and 16-17 on page 8 of the amendment.

There is insufficient antecedent basis for this limitation in the claim.

g) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 18-19 and 26-27 on page 10 and lines 1-2 on page 11 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

h) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 20-21 and 28-29 on page 10 and lines 3-4 on page 11 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

i) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 22-23 and 30-31 on page 10 and lines 5-6 on page 11 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

j) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 24-25 and 32-33 on page 10 and lines 7-8 on page 11 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

k) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 10-11, 14-15 and 18-19 on page 11 of the amendment.

There is insufficient antecedent basis for this limitation in the claim.

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- l) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 12-13, 16-17 and 20-21 on page 11 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- m) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 20-21 and 28-29 on page 13 and lines 3-4 on page 14 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- n) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 22-23 and 30-31 on page 13 and lines 5-6 on page 14 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- o) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 24-25 and 32-33 on page 13 and lines 7-8 on page 14 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- p) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 26-27 on page 13 and lines 1-2 and 9-10 on page 14 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- q) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 12-13, 16-17 and 20-21 on page 14 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- r) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 14-15, 18-19 and 22-23 on page 14 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

- s) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 23-24 and 31-32 on page 16 and lines 7-8 on page 17 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- t) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 25-26 on page 16 and lines 1-2 and 7-8 on page 17 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- u) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 27-28 on page 16 and lines 3-4 and 9-10 on page 17 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- v) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 29-30 on page 16 and lines 5-6 and 13-14 on page 17 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- w) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 16-17, 20-21 and 24-25 on page 17 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- x) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 18-19, 22-23 and 26-27 on page 17 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- y) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 25-26 on page 19 and lines 1-2 and 9-10 on page 20 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

- z) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 27-28 on page 19 and lines 3-4 and 11-12 on page 20 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- aa) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 29-30 on page 19 and lines 5-6 and 13-14 on page 20 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- ab) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 31-32 on page 19 and lines 7-8 and 15-16 on page 20 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- ac) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 18-19, 22-23 and 26-27 on page 20 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- ad) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 20-21, 24-25 and 28-29 on page 20 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- ae) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 29-30 on page 22 and lines 5-6 and 13-14 on page 23 of the amendment. There is insufficient antecedent basis for this limitation in the claim.
- af) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 31-32 on page 22 and lines 7-8 and 15-16 on page 23 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

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ag) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 1-2, 9-10 and 17-18 on page 23 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

ah) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 3-4, 11-12 and 19-20 on page 23 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

ai) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 22-23, 26-27 and 30-31 on page 23 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

aj) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 24-25, 28-29 and 32-33 on page 23 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

ak) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 31-32 on page 25 and lines 7-8 and 15-16 on page 26 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

al) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 1-2, 9-10 and 17-18 on page 26 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

am) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 3-4, 11-12 and 19-20 on page 26 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

an) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 5-6, 13-14 and 21-22 on page 26 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

ao) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 24-25, 28-29 and 32-33 on page 26 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

ap) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 26-27 and 30-31 on page 26 and lines 1-2 on page 27 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

aq) Claim 7 recites the limitation "1-methyl" in the nomenclature of the species spanning lines 2-3, 10-11 and 18-19 on page 29 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

ar) Claim 7 recites the limitation "2-methyl" in the nomenclature of the species spanning lines 4-5, 12-13 and 20-21 on page 29 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

as) Claim 7 recites the limitation "4-methyl" in the nomenclature of the species spanning lines 6-7, 14-15 and 22-23 on page 29 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

at) Claim 7 recites the limitation "5-methyl" in the nomenclature of the species spanning lines 8-9, 16-17 and 24-25 on page 29 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

au) Claim 7 recites the limitation "1,5-dimethyl" in the nomenclature of the species spanning lines 28-29 and 32-33 on page 29 and lines 3-4 on page 30 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

av) Claim 7 recites the limitation "2,4-dimethyl" in the nomenclature of the species spanning lines 30-31 on page 29 and lines 1-2 and 5-6 on page 30 of the amendment. There is insufficient antecedent basis for this limitation in the claim.

aw) Claim 20 is vague and indefinite in that it is not known what is meant by behavioral in line 7 on page 32 of the amendment.

Allowable Subject Matter

9. Claims 8, 11 and 12 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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A handwritten signature in cursive script that reads "Brenda Coleman". The signature is written in black ink and includes a long, horizontal flourish at the end.

Brenda Coleman
Primary Examiner Art Unit 1624
July 14, 2004